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Abstract 2971 Bendamustine As Salvage Therapy in Multiple Myeloma: A Retrospective, Multicenter Study From the Italian Compassionate Use Program in 78 Heavily Pre-Treated Patients

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Introduction: Bendamustine is a bifunctional alkylating agent approved for the treatment of several lymphoproliferative disorders. Studies have evidenced its efficacy in multiple myeloma (MM), but data so far available in this setting are scarce. We performed a retrospective analysis of Italian patients with relapsed/refractory MM, who had received bendamustine as salvage therapy within a national compassionate use program. Patients and methods: Seventy-eight patients (42 males, 36 females) were collected in 19 hematological centers. Mean age was 64.2 years (range 38-84). ISS was equally distributed, with about one third of patents being represented in single stages. Twenty-three of 43 analyzed patients had cytogenetic abnormalities, the most frequent being del13q (14 patients); t(4;14) and t(11;14) were observed in 4 and 2 patients, respectively, while t(6;14), del17p or complex karyotype occurred in single patients. The median number of prior lines of therapy was 4 (range 1-10). Ninety-seven percent of patients had previously received bortezomib, 94% IMIDs, 85% melphalan, 74% cyclophosphamide, 45% anthracyclines, 26% other drugs, 33% radiotherapy. Sixty percent of patients had undergone autologous and 4% allogeneic stem cell transplantation. The last treatment

before bendamustine was a bortezomib-based regimen in 31%, an IMIDs-based regimen in 42%, a combined bortezomib/IMIDs-based regimen in 9%, while 18% of patients had received other therapies. Seventy-three percent of patients were resistant to last therapy received, while 27% had relapsed. Median duration of response to last treatment received before bendamustine was 9 months (range 2-46). Median Hb value was 10.1 g/dl (range 7.6-14.9), WBC count 2.700/µl (range 550-15.200), PLT count 130.000/µl (range 6.000-410.000). Serum creatinine, calcium, beta2-microglobulin and LDH levels were increased in 12 (15%), 4 (5%), and 44 (56%) patients, respectively, while albumin levels were decreased in 27 patients (35%). The median percentage of marrow plasma cells (as evaluated in 57 cases) was 60% (range 1-100). Seventy-six percent of patients had osteolytic bone involvement and 78% extramedullary localizations, with 13% showing secondary plasma cell leukemia and 7% documented amyloidosis or proteinuria. Finally, 45% of patients presented with at least one severe comorbidity, mainly cardio-vascular, liver or pulmonary dysfunction, and diabetes. Results: A total of 236 cycles was administered (median 3, range 1-9). In 47% of patients bendamustine was variously associated to bortezomib (23%), or IMIDs (21%), or to a combination of both (3%). In 80% of patients receiving bendamustine +/- steroids, a median dose of 90 mg/sqm for two consecutive days every 28 days was employed; the median dose was 80 mg/sqm when bendamustine was combined with bortezomib, 60 mg/sqm with IMIDs (total range: 40-140 mg/sqm). The remaining patients received single, monthly doses ranging from 60 to 150 mg/sqm. According to IMWG uniform response criteria, 21 out of 73 evaluable patients achieved a response after a median time of 3 months. In particular, there were 16 PR, 1 VGPR,1 sCR, and 3 CR; overall response rate (ORR) was, therefore, 29%. Response rate was 10% (4/39) in bendamustine single agent +/- steroids, 38% (5/13) in bendamustine + bortezomib and 62% (10/16) in bendamustine + IMIDs subgroups, respectively. Responders had received a lower number of previous treatments than non responders (median 3 vs 4). Response rate was higher in relapsed (12/21, 57%) than in resistant patients (10/57, 17%). The time to best response ranged from 1 to 8 months. After a median follow-up of 8 months, median PFS duration was 6 months, with 13 out of 21 responding patients not yet progressed. Median OS of the entire cohort was 6.2 months (7 months in responders and 4 months in non responders, range 0-27). Grade 3-4 hematological and non-hematological toxicities occurred in 56% and 15% of patients, respectively, causing three interruptions of the treatment. Conclusions: Though with the clear limits due to the high heterogeneity of treatments applied and of population analyzed, our data indicate that bendamustine may be a therapeutic option in heavily pretreated MM, suggesting a possible non cross-resistance with other agents. Its earlier use with appropriate doses and combinations might further improve the results obtained in this study.

Disclosures: Musto: *Mundipharma:* Honoraria. **Off Label Use:** Bendamustine in relapsed/refractory myeloma. **Fragasso:** *Mundipharma:* Honoraria. **Baldini:** *Mundipharma:* Honoraria. **Storti:** *Mundipharma:* Honoraria.